
Depleting dietary valine permits nonmyeloablative mouse hematopoietic stem cell transplantation.

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Public Summary:

Blood or hematopoietic stem cells (HSCs) live within the bone marrow and are responsible for maintaining life-long blood formation. Bone marrow or HSC transplantation is used clinically to cure patient of a range of blood diseases. A key step in this therapy is the depletion of the recipient's HSCs from the bone marrow in order to make space for donor HSCs to engraft, and is usually achieved by toxic chemotherapy or radiation. Here we report that the essential amino acid valine is indispensable for the maintenance of HSCs. Dietary valine restriction emptied the mouse bone marrow of HSCs, affording donor-HSC engraftment without chemotherapy/radiation conditioning. These findings suggest a new metabolic approach in HSC transplantation.

Scientific Abstract:

A specialized bone marrow microenvironment (niche) regulates hematopoietic stem cell (HSC) self-renewal and commitment. For successful donor-HSC engraftment, the niche must be emptied via myeloablative irradiation or chemotherapy. However, myeloablation can cause severe complications and even mortality. Here we report that the essential amino acid valine is indispensable for the proliferation and maintenance of HSCs. Both mouse and human HSCs failed to proliferate when cultured in valine-depleted conditions. In mice fed a valine-restricted diet, HSC frequency fell dramatically within 1 week. Furthermore, dietary valine restriction emptied the mouse bone marrow niche and afforded donor-HSC engraftment without chemoradiative myeloablation. These findings indicate a critical role for valine in HSC maintenance and suggest that dietary valine restriction may reduce iatrogenic complications in HSC transplantation.

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